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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/927,161 | 08/10/2001 | Maria R. Díaz-Torres | GC627-2 | 3999 |

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GENENCOR INTERNATIONAL, INC.
ATTENTION: LEGAL DEPARTMENT
925 PAGE MILL ROAD
PALO ALTO, CA 94304

EXAMINER

BYRD, DEVON R.

| | |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1639;

DATE MAILED: 10/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/927,161

Applicant(s)

DIAZ-TORRES ET AL.

Examiner

Devon R Byrd

Art Unit

1639

FILE
COPY

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8 & 9.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

STATUS OF THE CLAIMS

CLAIMS 1-19 ARE PENDING IN THIS APPLICATION AND ARE SUBJECT TO RESTRICTION/ELECTION OF SPECIES. CLAIMS 1-12 ARE UNDER CONSIDERATION. CLAIMS 13-19 ARE WITHDRAWN FROM CONSIDERATION.

ELECTION/RESTRICTION

APPLICANT'S ELECTION WITH TRAVERSE OF GROUP 1 (CLAIMS 1-12) IN PAPER NO. 12 IS ACKNOWLEDGED. CLAIMS 13-19 ARE WITHDRAWN FROM FURTHER CONSIDERATION PURSUANT TO 37 CFR 1.142(b), AS BEING DRAWN TO A NONELECTED INVENTION, THERE BEING NO ALLOWABLE GENERIC OR LINKING CLAIM. APPLICANT TIMELY TRAVERSED THE RESTRICTION (ELECTION) REQUIREMENT IN PAPER NO. 12.

APPLICANT'S ELECTION WITHOUT TRAVERSE OF THE SPECIES "BACILLUS" IN PAPER NO. 12 IS ACKNOWLEDGED.

APPLICANT IS REMINDED THAT UPON THE CANCELLATION OF CLAIMS TO A NON-ELECTED INVENTION, THE INVENTORSHIP MUST BE AMENDED IN COMPLIANCE WITH 37 CFR 1.48(b) IF ONE OR MORE OF THE CURRENTLY NAMED INVENTORS IS NO LONGER AN INVENTOR OF AT LEAST ONE CLAIM REMAINING IN THE APPLICATION. ANY AMENDMENT OF INVENTORSHIP MUST BE ACCOMPANIED BY A REQUEST UNDER 37 CFR 1.48(b) AND BY THE FEE REQUIRED UNDER 37 CFR 1.17(ii).

INFORMATION DISCLOSURE STATEMENT

THE INFORMATION DISCLOSURE STATEMENT FILED NOVEMBER 8, 2002 (PAPER NO. 9) FAILS TO COMPLY WITH 37 CFR 1.98(a)(2), WHICH REQUIRES A LEGIBLE COPY OF EACH U.S. AND FOREIGN PATENT; EACH PUBLICATION OR THAT PORTION WHICH CAUSED IT TO BE LISTED; AND

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ALL OTHER INFORMATION OR THAT PORTION WHICH CAUSED IT TO BE LISTED. THE CROSSED OUT REFERENCE, NOT PROVIDED BY APPLICANT, HAS NOT BEEN CONSIDERED.

CLAIM OBJECTIONS

CLAIM 12 RECITES THE LIMITATION "THE HOMOLOGY" IN LINE 3. THERE IS INSUFFICIENT ANTECEDENT BASIS FOR THIS LIMITATION IN THE CLAIM. APPROPRIATE CORRECTION IS REQUIRED.

CLAIM REJECTIONS - 35 USC § 112, 2ND PARAGRAPH

THE FOLLOWING IS A QUOTATION OF THE SECOND PARAGRAPH OF 35 U.S.C. 112:

THE SPECIFICATION SHALL CONCLUDE WITH ONE OR MORE CLAIMS PARTICULARLY POINTING OUT AND DISTINCTLY CLAIMING THE SUBJECT MATTER WHICH THE APPLICANT REGARDS AS HIS INVENTION.

CLAIMS 1-12 ARE REJECTED UNDER 35 U.S.C. 112, SECOND PARAGRAPH, AS BEING INDEFINITE FOR FAILING TO PARTICULARLY POINT OUT AND DISTINCTLY CLAIM THE SUBJECT MATTER WHICH APPLICANT REGARDS AS THE INVENTION. THE TERM "SELECTING" IN THE PHRASE "SELECTING A COMPETENT MICROORGANISM" RENDERS THE CLAIM INDEFINITE. IT IS UNCLEAR WHETHER THE TERM IS INTENDED TO REFER TO (A) CHOOSING ONE COMPETENT MICROORGANISM FROM AMONG A PLURALITY OF COMPETENT MICROORGANISMS; (B) IMPOSING A GENETIC SELECTION ON A [POPULATION OF] COMPETENT MICROORGANISMS; (C) PRODUCING A COMPETENT MICROORGANISM THROUGH A PROCESS OF GENETIC SELECTION; OR (D) SOMETHING ELSE ENTIRELY.

CLAIM 12 IS REJECTED UNDER 35 U.S.C. 112, SECOND PARAGRAPH, AS BEING INDEFINITE FOR FAILING TO PARTICULARLY POINT OUT AND DISTINCTLY CLAIM THE SUBJECT MATTER WHICH APPLICANT REGARDS AS THE INVENTION. THE TERM "INCREASING" IN THE PHRASE "...INCREASING THE HOMOLOGY BETWEEN SAID TARGET SEQUENCE AND SAID DNA CONSTRUCT" IS A RELATIVE TERM THAT RENDERS THE CLAIM INDEFINITE. THE TERM IS NOT DEFINED BY THE CLAIM,

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THE SPECIFICATION DOES NOT PROVIDE A STANDARD FOR ASCERTAINING THE REQUISITE DEGREE, AND ONE OF ORDINARY SKILL IN THE ART WOULD NOT BE REASONABLY APPRISED OF THE SCOPE OF THE INVENTION. THE CLAIM PARAMETER OF "HOMOLOGY" HAS BEEN RENDERED INDEFINITE BECAUSE THERE ARE NEITHER QUANTITATIVE NOR QUALITATIVE REFERENTS FOR "INCREASING". FROM WHAT INITIAL STATE OR VALUE IS HOMOLOGY BEING INCREASED? IN OTHER WORDS, INCREASED COMPARED TO WHAT? WHAT ASPECT OF HOMOLOGY IS BEING INCREASED? IS IT THE DEGREE OF HOMOLOGY? IS IT THE LENGTH OF HOMOLOGOUS SEQUENCE? IS IT BOTH?

IT IS NOTED THAT EXAMPLE 5 OF THE SPECIFICATION DISCLOSES "...VARYING THE SIZE OF THE HOMOLOGY BOX" (EMPHASIS ADDED). HOWEVER, CLAIM 12 DOES NOT RECITE THESE LIMITATIONS.

CLAIM REJECTIONS - 35 USC § 112, 1ST PARAGRAPH

(WRITTEN DESCRIPTION)

THE FOLLOWING IS A QUOTATION OF THE FIRST PARAGRAPH OF 35 U.S.C. 112:

THE SPECIFICATION SHALL CONTAIN A WRITTEN DESCRIPTION OF THE INVENTION, AND OF THE MANNER AND PROCESS OF MAKING AND USING IT, IN SUCH FULL, CLEAR, CONCISE, AND EXACT TERMS AS TO ENABLE ANY PERSON SKILLED IN THE ART TO WHICH IT PERTAINS, OR WITH WHICH IT IS MOST NEARLY CONNECTED, TO MAKE AND USE THE SAME AND SHALL SET FORTH THE BEST MODE CONTEMPLATED BY THE INVENTOR OF CARRYING OUT HIS INVENTION.

WITH REGARD TO THE DESCRIPTION REQUIREMENT, APPLICANTS' ATTENTION IS DIRECTED TO THE COURT OF APPEALS FOR THE FEDERAL CIRCUIT WHICH HELD THAT A "WRITTEN DESCRIPTION OF AN INVENTION INVOLVING A CHEMICAL GENUS, LIKE A DESCRIPTION OF A CHEMICAL SPECIES, 'REQUIRES A PRECISE DEFINITION, SUCH AS BY STRUCTURE, FORMULA [OR] CHEMICAL NAME,' OF THE CLAIMED SUBJECT MATTER SUFFICIENT TO DISTINGUISH IT FROM OTHER MATERIALS."

UNIVERSITY OF CALIFORNIA V. ELI LILLY AND Co., 43 USPQ2d 1398, 1405 (1997), QUOTING *FIER'S V. REVEL*, 25 USPQ2d 1601, 1606 (FED. CIR. 1993) (BRACKETED

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MATERIAL IN ORIGINAL) [THE CLAIMS AT ISSUE IN *UNIVERSITY OF CALIFORNIA V. ELI LILLY* DEFINED THE INVENTION BY FUNCTION OF THE CLAIMED DNA (ENCODING INSULIN)].

ALTHOUGH DIRECTED TO DNA COMPOUNDS, THIS HOLDING WOULD BE DEEMED TO BE APPLICABLE TO A GENERIC OF COMPOUNDS; WHICH REQUIRES A REPRESENTATIVE SAMPLE OF COMPOUNDS AND/OR A SHOWING OF SUFFICIENT IDENTIFYING CHARACTERISTICS TO DEMONSTRATE POSSESSION OF THE COMPOUND OR GENERIC(S). FOR EXAMPLE, IN A RECENT COURT CASE IN LINE WITH *ELI LILLY*, JUDGE LOURIE WRITING FOR THE CAFC MADE THE FOLLOWING OBSERVATION:

"A DESCRIPTION OF AN ANTI-INFLAMMATORY STEROID, I.E., A STEROID (A GENERIC STRUCTURAL TERM) HAVING THE FUNCTION OF LESSENING INFLAMMATION OF TISSUES, FAILS TO DISTINGUISH ANY STEROID FROM OTHERS HAVING THE SAME ACTIVITY OR FUNCTION. SIMILARLY, THE EXPRESSION "AN ANTIBIOTIC PENICILLIN" FAILS TO DISTINGUISH A PARTICULAR PENICILLIN MOLECULE FROM OTHERS POSSESSING THE SAME ACTIVITY."

SEE: J. LOURIE DECISION IN *ENZO BIOCHEM, INC. V. GEN-PROBE INC. ET AL.* No. 01-1230 (CAFC: DECIDED APRIL 2, 2002) (CITATION FORTHCOMING).

IN THIS REGARD, APPLICANT IS REFERRED TO THE SEMINAL CASE OF *UNIVERSITY OF CALIFORNIA V. ELI LILLY & CO.*, 119 F.3d 1559, 43 USPQ2d 1398 (FED. CIR. 1997) AND THE "GUIDELINES FOR EXAMINATION OF PATENT APPLICATIONS UNDER THE 35 USC 112, FIRST PARAGRAPH, 'WRITTEN DESCRIPTION' REQUIREMENT" PUBLISHED IN 1242 OG 168-178 (JANUARY 30, 2001).

IT IS NOTED THAT WRITTEN DESCRIPTION IS LEGALLY DISTINCT FROM ENABLEMENT:

"ALTHOUGH THE TWO CONCEPTS OF ARE ENTWINED, THEY ARE DISTINCT AND EACH IS EVALUATED UNDER SEPARATE LEGAL CRITERIA. THE WRITTEN DESCRIPTION REQUIREMENT, A QUESTION OF FACT, ENSURES THAT THE INVENTOR CONVEYS TO OTHERS THAT HE OR SHE HAD POSSESSION OF THE CLAIMED INVENTION; WHEREAS, THE ENABLEMENT REQUIREMENT, A QUESTION OF LAW,

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ENSURES THAT THE INVENTOR CONVEYS TO OTHERS HOW TO MAKE AND USE THE CLAIMED INVENTION." SEE 1242 OG 169 (JANUARY 30, 2001) CITING *UNIVERSITY OF CALIFORNIA V. ELI LILLY & CO.*

CLAIMS 1-12 ARE REJECTED UNDER 35 U.S.C. 112, FIRST PARAGRAPH, AS FAILING TO COMPLY WITH THE WRITTEN DESCRIPTION REQUIREMENT. THE CLAIM(S) CONTAINS SUBJECT MATTER THAT WAS NOT DESCRIBED IN THE SPECIFICATION IN SUCH A WAY AS TO REASONABLY CONVEY TO ONE SKILLED IN THE RELEVANT ART THAT THE INVENTOR(S), AT THE TIME THE APPLICATION WAS FILED, HAD POSSESSION OF THE CLAIMED INVENTION. (LACK OF WRITTEN DESCRIPTION)

CLAIMS 1-12 ARE DRAWN TO A METHOD FOR PRODUCING A TRANSFORMED MICROORGANISM VIA CHROMOSOMAL INTEGRATION OF EXOGENOUS DNA. THE CLAIMS ARE DRAWN TO ANY METHOD OF PRODUCING ANY DNA CONSTRUCT IN VITRO AND TRANSFORMING ANY COMPETENT MICROORGANISM WITH SAID CONSTRUCT, WHEREIN THE CONSTRUCT BECOMES INTEGRATED AT ANY POSITION OF ANY CHROMOSOME OF A MICROORGANISM. CONSEQUENTLY, THE SCOPE OF THESE CLAIMS IS ENORMOUS BECAUSE THEY WOULD INCLUDE AN INFINITE NUMBER OF METHODS FOR PRODUCING AN INFINITE NUMBER OF STRUCTURAL VARIANTS THAT ARE COMBINED TOGETHER TO FORM THE ULTIMATE PRODUCT (A TRANSFORMED MICROORGANISM). THE SPECIFICATION AND CLAIMS DO NOT PLACE ANY LIMIT ON THE NUMBER, TYPE, OR METHOD BY WHICH SAID STRUCTURAL VARIANTS MIGHT BE COMBINED.

ALTHOUGH THE SPECIFICATION DISCLOSES EXAMPLES DIRECTED TO CERTAIN METHODS OF TRANSFORMATION OF *BACILLUS SUBTILIS* (SEE SPECIFICATION, P 19, LN 16), THE SPECIFICATION AND CLAIMS DO NOT PROVIDE ANY GUIDANCE AS TO WHAT STRUCTURAL FEATURES ALL OF THE CLAIMED VARIANTS MIGHT SHARE; I.E., PROVIDING EXAMPLES OF "*BACILLUS [SUBTILIS]*" VARIANTS

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DOES NOT SUFFICIENTLY DESCRIBE VARIANTS THAT DO NOT FALL WITHIN THE "BACILLUS" CLASS AND ITS SPECIFIC SUBCLASSES (PLEASE NOTE: APPLICANTS' CLAIMS WOULD ENCOMPASS AN INFINITE NUMBER OF VARIANTS IN VIRTUALLY EVERY CLASS AND SUBCLASS).

CONSEQUENTLY, THERE IS NO TEACHING THAT WOULD ALLOW A PERSON OF SKILL IN THE ART TO DETERMINE *A PRIORI* THAT APPLICANTS WERE IN POSSESSION OF THE FULL SCOPE OF THE CLAIMED INVENTION AT THE TIME OF FILING BECAUSE THERE IS NO COMMON STRUCTURAL ATTRIBUTES THAT CAN LINK TOGETHER ALL OF THE CLAIMED METHOD VARIANTS.

THE GENERAL KNOWLEDGE AND LEVEL OF SKILL IN THE ART DO NOT SUPPLEMENT THE OMITTED DESCRIPTION BECAUSE SPECIFIC, NOT GENERAL, GUIDANCE IS WHAT IS NEEDED. SINCE THE DISCLOSURE FAILS TO DESCRIBE THE COMMON ATTRIBUTES OR CHARACTERISTICS THAT IDENTIFY ALL OF THE MEMBERS OF THE GENUS OR EVEN A SUBSTANTIAL PORTION THEREOF, AND BECAUSE THE GENUS IS ENORMOUS AND HIGHLY DIVERSE, LISTING EXAMPLES LIKE "BACILLUS" VARIANTS (SEE SPECIFICATION, SUMMARY OF THE INVENTION) IS INSUFFICIENT TO TEACH THE ENTIRE GENUS. CONSEQUENTLY, ONE OF SKILL IN THE ART WOULD REASONABLY CONCLUDE THAT THE DISCLOSURE FAILS TO PROVIDE A REPRESENTATIVE NUMBER OF SPECIES TO DESCRIBE THIS ENORMOUS GENUS. THUS, APPLICANT WAS NOT IN POSSESSION OF THE CLAIMED GENUS.

CLAIM 12 IS REJECTED UNDER 35 U.S.C. 112, FIRST PARAGRAPH, AS FAILING TO COMPLY WITH THE WRITTEN DESCRIPTION REQUIREMENT. THE CLAIM(S) CONTAINS SUBJECT MATTER THAT WAS NOT DESCRIBED IN THE SPECIFICATION IN SUCH A WAY AS TO REASONABLY CONVEY TO ONE SKILLED IN THE RELEVANT ART THAT THE INVENTOR(S), AT THE TIME THE APPLICATION WAS FILED, HAD POSSESSION OF THE CLAIMED INVENTION. (LACK OF WRITTEN DESCRIPTION)

CLAIM 12 IS DRAWN TO THE USE OF "INCREASING THE HOMOLOGY BETWEEN [A] TARGET SEQUENCE AND [A] DNA CONSTRUCT" FOR USE IN A METHOD OF PRODUCING A TRANSFORMED

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ORGANISM. HOWEVER, THE METES AND BOUNDS OF THE STRUCTURES AND METHOD STEPS ENCOMPASSED BY THE ENQUOTED TERM ARE UNCLEAR.

DNA HOMOLOGY IS DEFINED AS "THE DEGREE OF SIMILARITY (RELATEDNESS) BETWEEN BASE SEQUENCES IN DIFFERENT DNA MOLECULES (OR IN DIFFERENT PARTS OF THE SAME MOLECULE); TWO NUCLEIC ACID MOLECULES WHICH ARE 100% HOMOLOGOUS HAVE IDENTICAL SEQUENCES OF NUCLEOTIDES". ("DICTIONARY OF MICROBIOLOGY AND MOLECULAR BIOLOGY", 2ND ED., SINGLETON ET AL., JOHN WILEY AND SONS, PRINTED 1995(SEE APPLICANT'S INFORMATION DISCLOSURE STATEMENT, PAPER NO. 9)). THUS, DNA HOMOLOGY IS DEFINED IN TERMS OF THE IDENTITY OF BASE ORDER BETWEEN TWO (OR MORE) SEQUENCES, RATHER THAN THE EXTENT (LENGTH OF) OF SEQUENCES COMPRISING BASE ORDER OF A GIVEN IDENTITY. FOR EXAMPLE, TWO 10 BASE PAIR LONG DNA MOLECULES THAT HAVE 8 BASE PAIRS IN COMMON ARE 80% HOMOLOGOUS. LIKewise, TWO 1,000,000 BASE PAIR LONG DNA MOLECULES THAT HAVE 800,000 BASE PAIRS IN COMMON ARE ALSO 80% HOMOLOGOUS.

THE SPECIFICATION, WHILE LACKING AN EXPLICIT DESCRIPTION DEFINING THE TERM "HOMOLOGY", SEEMS TO DEFINE APPARENTLY RELATED TERMS IN DIFFERENT WAYS:

HOMOLOGOUS SEQUENCE- "... IS A SEQUENCE THAT IS FOUND IN THE SAME GENETIC SOURCE OR SPECIES. FOR EXAMPLE, THE HOST CELL STRAIN MAY BE DEFICIENT IN A SPECIFIC GENE. IF THAT GENE IS FOUND IN OTHER STRAINS OF THE SAME SPECIES THE GENE WOULD BE CONSIDERED A HOMOLOGOUS SEQUENCE."

THIS DEFINITION IS CONFUSING BECAUSE: (A) THERE IS NO MENTION OF SEQUENCE IDENTITY/SIMILARITY, (B) THE EXPLICIT DEFINITION (THE FIRST SENTENCE) READS ON ANY [DNA] SEQUENCE FOUND IN THE SAME SPECIES, IRRESPECTIVE OF THE DEGREE OF SEQUENCE IDENTITY, AND (C) THE MEANING OF "SAME GENETIC SOURCE" IS UNCLEAR, ESPECIALLY SINCE IT IS CAST IN THE ALTERNATIVE TO THE TERM "SPECIES". THE EXAMPLE CONFUSES THE ISSUE EVEN MORE

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BECAUSE THE MEANING OF THE TERM "DEFICIENT" IS UNCLEAR. DOES IT MEAN "FUNCTIONALLY DEFICIENT" (I.E., THE GENE AT ISSUE CONTAINS A NON- OR MIS-SENSE MUTATION IN THE CODING REGION, OR AN INACTIVATING MUTATION IN THE PROMOTER REGION, OR PERHAPS A DELETION MUTATION)? DOES IT MEAN THAT THE GENE AT ISSUE IS ABSENT ENTIRELY (I.E., THE ORGANISM LACKS A GENE THAT CONFERS RESISTANCE TO ERYTHROMYCIN, OR PERHAPS A PLASMID THAT CONFERS A PATHOGENIC PHENOTYPE, E.G., B. CEREUS VIS-À-VIS B. ANTHRACIS)? IN THE CASE WHEREIN THE GENE AT ISSUE IS ABSENT ENTIRELY, WHAT IS THE MEANING OF THE TERM "THAT GENE" AS "A HOMOLOGOUS SEQUENCE" SINCE NO SEQUENCE IDENTITY IS POSSIBLE TO A GENE THAT IS ABSENT? *FURTHERMORE, EXEMPLIFICATION DOES NOT CONSTITUTE EXPLICIT DEFINITION.*

HOMOLOGY BOX- "... MAY FLANK EACH SIDE OF THE INCOMING SEQUENCE. THE SEQUENCE OF EACH HOMOLOGY BOX IS HOMOLOGOUS TO A SEQUENCE IN THE BACILLUS CHROMOSOME. THESE SEQUENCES DIRECT WHERE IN THE BACILLUS CHROMOSOME THE NEW CONSTRUCT GETS INTEGRATED AND WHAT PART OF THE BACILLUS [SIC] CHROMOSOME WILL BE REPLACED BY THE INCOMING SEQUENCE".

THIS DEFINITION IS CONFUSING BECAUSE IT RELIES UPON THE DEFINITION OF "HOMOLOGOUS SEQUENCE" DISCUSSED ABOVE. MOREOVER, IT IS EXPLICITLY DIRECTED TO MODIFICATION OF BACILLUS CHROMOSOMES AND IS THEREFORE NOT COMMENSURATE WITH THE VAST SCOPE OF THE CLAIMS.

APPLICANTS DO NOT PROVIDE A SINGLE EXAMPLE THAT EXPLICITLY DESCRIBES AN INCREASE IN SEQUENCE IDENTITY BETWEEN A TARGET SEQUENCE AND A DNA CONSTRUCT. EXAMPLE 5 OF THE SPECIFICATION IS DIRECTED TO "...VARYING THE SIZE OF THE HOMOLOGY BOX", WHICH DOES NOT NECESSARILY ALTER THE PERCENT HOMOLOGY BETWEEN THE CONSTRUCT AND THE TARGET SEQUENCE. APPLICANT DEFINES "TARGET SEQUENCE" AS "... THE SEQUENCE WHERE IT IS DESIRED FOR THE INCOMING SEQUENCE TO BE INSERTED INTO THE ... GENOME. THE TARGET

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SEQUENCE MAY ENCODE A FUNCTIONAL WILD-TYPE GENE OR OPERON, A FUNCTIONAL MUTANT GENE OR OPERON, OR A NON-FUNCTIONAL GENE OR OPERON". THUS, THE "TARGET SEQUENCE" IS PHYSICALLY DEFINED BY THE EXTENT OF THE REGION OF THE CHROMOSOME THAT UNDERGOES RECOMBINATION. IN VIEW OF THE DEFINITION PROVIDED FOR "HOMOLOGY BOX", THE "TARGET SEQUENCE" IS IN TURN DEFINED BY THE COMPOSITION OF THE DNA CONSTRUCT. THE TERM DOES NOT APPEAR TO REFER TO THE CHROMOSOME AS A WHOLE, NOR A SUBSTANTIAL SEGMENT THEREOF.

EVEN IF IT WERE ARGUED THAT "TARGET SEQUENCE" INCLUDES THE CHROMOSOME AS A WHOLE OR A SUBSTANTIAL SEGMENT THEREOF, AND THEREFORE AN INCREASE IN THE SIZE OF A HOMOLOGY BOX WOULD CONSTITUTE AN INCREASE IN PERCENT SEQUENCE IDENTITY BETWEEN A TARGET SEQUENCE AND A DNA CONSTRUCT, APPLICANT'S EXAMPLE 4 WOULD APPEAR TO BE IN CONFLICT WITH CLAIM 12.

EXAMPLE 4 DESCRIBES AN INCREASE IN TRANSFORMATION EFFICIENCY BROUGHT ABOUT BY THE ADDITION OF NON-HOMOLOGOUS SEQUENCES TO THE DISTAL PORTIONS OF A DNA CONSTRUCT. SAID ADDITION WOULD ONLY DECREASE THE DEGREE OF SEQUENCE HOMOLOGY BETWEEN A TARGET SEQUENCE (IRRESPECTIVE OF HOW APPLICANT'S DEFINITION OF THAT TERM IS CONSTRUED) AND A DNA CONSTRUCT.

CLAIM REJECTIONS - 35 USC § 102

THE FOLLOWING IS A QUOTATION OF THE APPROPRIATE PARAGRAPHS OF 35 U.S.C. 102 THAT FORM THE BASIS FOR THE REJECTIONS UNDER THIS SECTION MADE IN THIS OFFICE ACTION:

A PERSON SHALL BE ENTITLED TO A PATENT UNLESS -

(B) THE INVENTION WAS PATENTED OR DESCRIBED IN A PRINTED PUBLICATION IN THIS OR A FOREIGN COUNTRY OR IN PUBLIC USE OR ON SALE IN THIS COUNTRY, MORE THAN ONE YEAR PRIOR TO THE DATE OF APPLICATION FOR PATENT IN THE UNITED STATES.

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CLAIMS 1-12 ARE REJECTED UNDER 35 U.S.C. 102(B) AS BEING ANTICIPATED BY HAHN ET AL., MOLECULAR MICROBIOLOGY 21(4): 763-775, 1996 (HEREINAFTER REFERRED TO AS HAHN).

THE INVENTION OF THE ABOVE CLAIM IS DRAWN TO A METHOD OF PRODUCING A TRANSFORMED MICROORGANISM COMPRISING THE DIRECT INTRODUCTION AND SUBSEQUENT CHROMOSOMAL INTEGRATION OF A DNA CONSTRUCT PRODUCED IN VITRO INTO A SELECTED COMPETENT MICROORGANISM, WHEREIN:

- THE MICROORGANISM IS A SUPER-COMPETENT PXYL-COMK STRAIN [OF BACILLUS]
- THE DNA CONSTRUCT COMPRISES
 - HOMOLOGOUS OR HETEROLOGOUS DNA
 - EITHER WILD-TYPE OR MODIFIED DNA
 - STUFFER SEGMENTS
 - A SEGMENT FLANKED BY HOMOLOGY BOXES
- THE DNA CONSTRUCT IS A NON-PLASMID DNA CONSTRUCT
- THE DNA CONSTRUCT IS PRODUCED WITHOUT THE USE OF A SHUTTLE VECTOR OR AN INTERMEDIATE HOST.
- THE HOMOLOGY BETWEEN THE TARGET SEQUENCE AND THE DNA CONSTRUCT IS INCREASED

HAHN TEACHES A METHOD OF PRODUCING A TRANSFORMED MICROORGANISM COMPRISING THE DIRECT INTRODUCTION AND SUBSEQUENT CHROMOSOMAL INTEGRATION OF A DNA CONSTRUCT PRODUCED IN VITRO INTO A SELECTED COMPETENT MICROORGANISM (P765, COL 1, 4TH PAR., AND 2ND COL, 1ST PAR.), WHEREIN:

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- THE MICROORGANISM IS A SUPER-COMPETENT (P 765, COL 1, 4TH PAR.) PXYL-COMK STRAIN OF BACILLUS (P 764, COL 1, 2ND PAR.)
- THE DNA CONSTRUCT COMPRISES HOMOLOGOUS AND HETEROLOGOUS DNA, WILD-TYPE AND MODIFIED DNA, STUFFER SEGMENTS, A SEGMENT FLANKED BY HOMOLOGY BOXES (P765, COL 1, 4TH PAR., AND 2ND COL, 1ST PAR.).
- THE DNA CONSTRUCT IS A NON-PLASMID DNA CONSTRUCT (P765, COL 2, 1ST PAR., LNS 6-7)
- THE DNA CONSTRUCT IS PRODUCED WITHOUT THE USE OF A SHUTTLE VECTOR OR AN INTERMEDIATE HOST (P765, COL 1, 4TH PAR., AND COL 2, 1ST PAR., LNS 6-7).
- THE HOMOLOGY BETWEEN THE TARGET SEQUENCE AND THE DNA CONSTRUCT IS INCREASED (P 772, 2ND COL, PAR. ENTITLED " CONSTRUCTION OF COMK-LACZ")

THEREFORE, ALL OF THE CLAIMED LIMITATIONS DISCUSSED ABOVE ARE ANTICIPATED BY HAHN.

CLAIMS 1-3, AND 6-9 ARE REJECTED UNDER 35 U.S.C. 102(B) AS BEING ANTICIPATED BY NIAUDET ET AL., JOURNAL OF BACTERIOLOGY 163(1): 111-120, 1985 (HEREINAFTER REFERRED TO AS NIAUDET).

NIAUDET TEACHES A METHOD OF PRODUCING A TRANSFORMED MICROORGANISM COMPRISING:

- SELECTING A COMPETENT MICROORGANISM, WHEREIN SAID MICROORGANISM IS A BACILLUS (P 111, LNS 7-8 UNDER "MATERIALS AND METHODS")
- PRODUCING A DNA CONSTRUCT IN VITRO, WHEREIN SAID DNA CONSTRUCT FURTHER COMPRISES STUFFER SEQUENCES (P 113, LNS 1-5 OF SECTION ENTITLED "TRANSFORMING DNA MOLECULES", AND FIGURE 1)

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- DIRECTLY TRANSFORMING SAID MICROORGANISM WITH SAID DNA CONSTRUCT SUCH THAT THE DNA CONSTRUCT BECOMES INTEGRATED INTO A CHROMOSOME OF SAID MICROORGANISM (P 113, COL 2, ENTIRE MIDDLE PAR. (BEGINS: "PHV453 TRANSFORMED B. SUBTILIS EFFICIENTLY...")
- WHEREIN SAID DNA CONSTRUCT COMPRISES HOMOLOGOUS AND HETEROLOGOUS SEQUENCES (P 112, LNS 1-4 UNDER "RESULTS" SECTION, AND FIGURE 4A)

THEREFORE, ALL OF THE CLAIMED LIMITATIONS DISCUSSED ABOVE ARE ANTICIPATED BY NIAUDET.

CLAIMS 1-4, 5-7 10, AND 11 ARE REJECTED UNDER 35 U.S.C. 102(B) AS BEING ANTICIPATED BY VAN SINDEREN AND VENEMA, JOURNAL OF BACTERIOLOGY 176(18): 5762-5570, 1994 (HEREINAFTER REFERRED TO AS VENEMA).

VENEMA TEACHES A METHOD OF PRODUCING A TRANSFORMED MICROORGANISM COMPRISING THE DIRECT INTRODUCTION AND SUBSEQUENT CHROMOSOMAL INTEGRATION OF A DNA CONSTRUCT PRODUCED IN VITRO INTO A SELECTED COMPETENT MICROORGANISM, WHEREIN SAID DNA CONSTRUCT COMPRISES HOMOLOGOUS AND HETEROLOGOUS SEQUENCES (AS DEFINED IN APPLICANT'S SPECIFICATION, P 9, LNS 11-20), AND WHEREIN SAID MICROORGANISM IS A BACILLUS (P 5763, COL 1, PARAGRAPH ENTITLED CONSTRUCTION OF PLASMIDS, LNS 7-10).

VENEMA FURTHER TEACHES A METHOD OF PRODUCING A TRANSFORMED MICROORGANISM COMPRISING THE DIRECT INTRODUCTION AND SUBSEQUENT CHROMOSOMAL INTEGRATION OF A DNA CONSTRUCT PRODUCED IN VITRO, WHEREIN SAID DNA CONSTRUCT IS A NON-PLASMID DNA CONSTRUCT PRODUCED WITHOUT THE USE OF A SHUTTLE VECTOR OR AN INTERMEDIATE HOST, INTO A SELECTED COMPETENT MICROORGANISM, WHEREIN SAID MICROORGANISM IS A

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SUPER-COMPETENT BACILLUS (P 5767, FINAL PARAGRAPH OF "RESULTS" SECTION, LAST 15 LINES, AND FIGURES 8A & 8B).

THEREFORE, ALL OF THE CLAIMED LIMITATIONS DISCUSSED ABOVE ARE ANTICIPATED BY VENEMA.

CLAIMS 1-3, 6, 7, 10, 11 ARE REJECTED UNDER 35 U.S.C. 102(B) AS BEING ANTICIPATED BY US PATENT 4,828,994, ISSUED MAY 9, 1989 (HEREINAFTER REFERRED TO AS '994).

'994 TEACHES A METHOD OF PRODUCING A TRANSFORMED MICROORGANISM COMPRISING THE DIRECT INTRODUCTION AND SUBSEQUENT CHROMOSOMAL INTEGRATION OF A DNA CONSTRUCT PRODUCED IN VITRO INTO A SELECTED COMPETENT MICROORGANISM, WHEREIN SAID DNA CONSTRUCT COMPRISES HOMOLOGOUS AND HETEROLOGOUS SEQUENCES (AS DEFINED IN APPLICANT'S SPECIFICATION, P 9, LNS 11-20) AND IS A NON-PLASMID DNA CONSTRUCT PRODUCED WITHOUT THE USE OF A SHUTTLE VECTOR OR AN INTERMEDIATE HOST, AND WHEREIN SAID MICROORGANISM IS A BACILLUS (COLS 10-11, EXAMPLES V AND VI).

THEREFORE, ALL OF THE CLAIMED LIMITATIONS DISCUSSED ABOVE ARE ANTICIPATED BY '994.

CLAIMS 1-3, 6, AND 7 ARE REJECTED UNDER 35 U.S.C. 102(B) AS BEING ANTICIPATED BY EPO761815A2, PUBLISHED DECEMBER 3, 1997 (HEREINAFTER REFERRED TO AS '815).

'815 TEACHES A METHOD OF PRODUCING A TRANSFORMED MICROORGANISM COMPRISING THE DIRECT INTRODUCTION (P 11, LNS 17-20) AND SUBSEQUENT CHROMOSOMAL INTEGRATION (P 11, LN 55- P 12, LN 1) OF A DNA CONSTRUCT PRODUCED IN VITRO (P 10,

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LNS 17 AND 37) INTO A SELECTED COMPETENT MICROORGANISM (P 11, 17), WHEREIN SAID DNA CONSTRUCT COMPRISES HOMOLOGOUS AND HETEROLOGOUS SEQUENCES (AS DEFINED IN APPLICANT'S SPECIFICATION, P 9, LNS 11-20) (P 6, LNS 11-26), AND WHEREIN SAID MICROORGANISM IS A BACILLUS (ENTIRE DOCUMENT).

THEREFORE, ALL OF THE CLAIMED LIMITATIONS DISCUSSED ABOVE ARE ANTICIPATED BY '815.

CONCLUSION

NO CLAIMS ARE ALLOWED.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DEVON R BYRD WHOSE TELEPHONE NUMBER IS 703-305-0159. THE EXAMINER CAN NORMALLY BE REACHED ON MON-FRI 8A-5P.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, ANDREW WANG CAN BE REACHED ON 703-306-2317. THE FAX PHONE NUMBER FOR THE ORGANIZATION WHERE THIS APPLICATION OR PROCEEDING IS ASSIGNED IS (703) 872-9306.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE RECEPTIONIST WHOSE TELEPHONE NUMBER IS 703-308-1235.

DB

OCTOBER 17, 2003

BENNETT CELSA
PRIMARY EXAMINER

